Regional covariance analysis of an event-related fMRI study investigating the neurobehavioral impact of sleep deprivation on performance of a delayed-match-to-sample task

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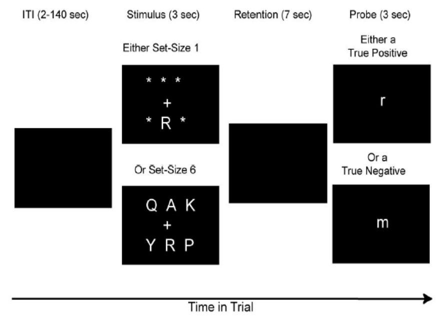
Introduction

The brain consists of a set of functionally distinct regions, which are interconnected to form functional networks. In this study we sought to identify sleep-deprivation induced changes to pre-existing functional networks that support basic psychomotor and short-term memory function. With this goal in mind, we chose to examine changes to the functional MR signal before and during profound sleep deprivation obtained while subjects performed a speeded short-term memory task closely related to the Sternberg paradigm. In addition to basic visual, motor, and short-term memory function, this paradigm also provides an internal manipulation of difficulty useful in addressing the specificity of the observed brain networks.

Methods

Eighteen healthy subjects, between the ages of 20 and 35 years (age = 26.3 ± 4.9 years), participated in an event-related functional magnetic resonance imaging (efMRI) paradigm of a delayed-match-to-sample (DMS) task. The trial events were: a 3 sec study period of either a 1,3, or 6-letter visual array; a 7 sec retention interval; and, a 3 sec probe period, where a button press indicated whether the probe letter was in the study array The initial scan occurred at 9 AM ("PRE"), and the follow-up scan occurred at the same time 48 hrs later ("POST") to eliminate confounding circadian effects, yielding 48 hours of prolonged wakefulness. All subjects were right-handed and carefully screened to ensure that they had no history of medical, psychiatric, neurological, or sleep disorder. Subjects were instructed to stop drinking caffeine 24 hours prior to study participation and for the duration of the study. All subjects passed substance abuse screening tests. Subjects were supervised at all times, and polysomnographic monitoring confirmed that they remained awake during the sleep deprivation period. Fourteen control subjects (age 23.93 ± 1.14) underwent the same protocol without being sleep deprived. Informed consent, as approved by the Internal Review Board of the College of Physicians and Surgeons of Columbia University, was obtained prior to study participation for all subjects.



Multivariate analysis

Ordinal Trend Canonical Variates Analysis (OrT CVA) was performed on the data from the probe phase for 6 items. This analysis is similar to other regional covariance analyses techniques, like Partial Least Squares, in that it applies principal components analysis (PCA) to the data matrix that is transformed using a matrix representing the experimental design. Utilizing each voxel, OrT CVA was designed to identify a covariance pattern in the functional MR signal the expression of which decreases for as many subjects as possible from PRE to POST sleep deprivation.

Results

The first principal component of the OrT CVA (accounting for 30 % of the variance) displayed ordinal trend properties. Seventeen of 18 subjects decreased their pattern expression ($p<0.001$), suggesting an unambiguous neural correlate of sleep deprivation. We verified that the activation differences associated with this pattern were due to sleep deprivation only, and not due to an order effect. We applied the sleep-deprivation related pattern to the data of 14 control subjects that were scanned while performing the DMS task 48 hours apart without undergoing sleep deprivation, and did not find any systematic increase or decrease in pattern expression from scan 1 to scan 2 for the control subjects, thus ruling out that order effects gave rise to the activation pattern in the first place. Furthermore, the subject expression of the sleep-deprivation pattern does not differ significantly between the groups in the well-rested state, (subjects on day 1 vs. controls on day 1: $p=0.95$, subjects on day 1 vs. controls on day 2: $p=0.73$; p-levels from two-tailed t-tests.). We then tested whether individuals' pattern expression correlated with individual's behavioral performance and found that the decrease in expression as a result of sleep deprivation was significant in predicting the drop in recognition accuracy ($R^2=0.27$, $p<0.05$) from day 1 to day 2. Furthermore, the decrease in the activation pattern's expression predicted the increase in intra-individual reaction variability from PRE to POST ($R^2=0.59$, $p<0.0005$).

We therefore successfully identified a sleep-deprivation related activation pattern in the probe phase of a delayed-match-to-sample task. Both correlation of pattern expression with performance decrements as well as location of brain areas involved suggest that this pattern reflects changes to spatial attention and early visual processing induced by sleep deprivation.